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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/504,280	02/15/2000	Mike A. Clark	phoe-0057	5368

7590 02/03/2004

Woodcock Washburn Kurtz
Mackiewicz & Norris LLP
One Liberty Place - 46th Floor
Philadelphia, PA 19103

EXAMINER

ROMEO, DAVID S

ART UNIT	PAPER NUMBER
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1647

DATE MAILED: 02/03/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/504,280

Applicant(s)

CLARK, MIKE A.

Examiner

David S Romeo

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 16 October 2003.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-8, 14-17 and 24 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-8, 14-17 and 24 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☒ Claim(s) 1-8, 14-17, 24 are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 13) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.
- a) ☐ The translation of the foreign language provisional application has been received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other:

DETAILED ACTION

The amendment filed 10/16/2003 has been entered. Claims 1-8, 14-17, 24 are pending. Applicant's election with traverse of group II and the species succinimidyl succinate in Paper No. 7 is acknowledged. Applicant timely traversed the restriction (election) requirement in Paper No. 7. Claims 1-8, 14-17, 24 are being examined to the extent that they read upon the elected invention and/or species.

Maintained Formal Matters, Objections, and/or Rejections:

Claim Rejections - 35 USC § 103

Claims 1-7, 14-17, 24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tsutsumi (AL, cited by Applicants) in view of Satake-Ishikawa (y17) and Ishikawa (n17).

Applicant argues that there is no motivation, teaching, or suggestion to combine the references, that the references fail to suggest the desirability of the combination, that Tsutsumi does not teach or suggest modifying TNF α with PEG having molecular weight higher than 5000, that Satake-Ishikawa fails to suggest the desirability of modifying rHuG-CSF with PEG having molecular weight higher than 10,000, that Ishikawa does not teach or describe the modification of rHuG-CSF with PEG having molecular weight higher than 10,000, that Ishikawa does not teach or suggest what the effect of modifying rHuG-CSF with PEG having molecular weight higher than 10,000 would be. Applicant's arguments have been fully considered but they are not persuasive.

Satake-Ishikawa discloses that modification with a larger PEG molecule is more effective to enhance the in vivo activity of rHuG-CSF and exemplifies this teaching with PEG(10,000)

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(Abstract). Accordingly, Satake-Ishikawa teaches the desirability and advantages of modifying a bioactive molecule with a larger molecular weight PEG, which provides a teaching, suggestion, or motivation to modify a bioactive molecule with a larger PEG molecule. One of ordinary skill in the art would have a reasonable expectation that enhancement of in vivo activity is proportional to size of the PEG molecule because Satake-Ishikawa discloses that modification with a larger PEG molecule is more effective to enhance the in vivo activity of rHuG-CSF.

Ishikawa teaches the modification of G-CSF with PEG (page 5, full paragraph 3). The molecular weight of the PEG used is from 500-20,000 (page 5, full paragraph 4). Accordingly, Ishikawa teaches 20,000 molecular weight PEG for the modification of a bioactive molecule.

One of ordinary skill in the art would be motivated to modify TNF α with 20,000 molecular weight PEG because there would be a reasonable expectation that 20,000 molecular weight PEG would be more effective to enhance the in vivo activity of TNF α than a smaller molecular weight PEG. Obviousness does not require absolute predictability, only a reasonable expectation of success, i.e., a reasonable expectation of obtaining similar properties.

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

Claims 1 and 8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tsutsumi (AL, cited by Applicants) in view of Satake-Ishikawa (y17) and Ishikawa (n17) as applied to claim 1 above and further in view of Mark (v17).

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Applicant argues that this rejection is based on the assumption that one of ordinary skill in the art would be motivated to combine Tsutsumi (AL) with Satake-Ishikawa (y17) and Ishikawa (n17), and that this assumption is incorrect. Applicant's arguments have been fully considered but they are not persuasive. The motivation, teaching, or suggestion to combine Tsutsumi (AL) with Satake-Ishikawa (y17) and Ishikawa (n17) is discussed above in the response to Applicant's traverse of the preceding rejection.

Claim Rejections - 35 USC § 112

Claims 1-4, 14-17, 24 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 1-4, 14-17, 24 are indefinite because they recite the term "TNF."

Applicant argues that when the claim language read in light of the specification, the teachings of the prior art, and the claim interpretation given by one of ordinary skill in the art at the time of invention, one of ordinary skill in the art would understand the meaning of the term "TNF." Applicant's arguments have been fully considered but they are not persuasive.

The specification intends the term "TNF" to encompass TNF proteins that have been mutated by deletion or alteration of amino acids without significantly impairing biological activity (paragraph bridging pages 5-6). However, this definition does not indicate what biological activities are intended. Thus, when read in light of the specification the metes and bounds of the term "TNF" are not clearly set forth. The fact that the instant specification does not identify that material element or combination of elements which is unique to, and, therefore,

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definitive of “TNF,” indicates that the metes and bounds are not clearly set forth. The second paragraph of 35 USC § 112 requires that the claims particularly point out and distinctly define the metes and bounds of the subject matter that will be protected by the patent grant.

Claim Rejections - 35 USC § 112

Claims 1, 3, 5-8, 14, 24 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Support for the limitation “range of 15,000 to about 40,000” cannot be found in the disclosure as originally filed, and the introduction of such a limitation raises the issue of new matter. Applicant argues that support for the limitation can be found at page 7, lines 3-8, and in Example 3. Applicant's arguments have been fully considered but they are not persuasive. The specification at page 7, lines 3-8, and in Example 3 neither recites the limitation “range of 15,000 to about 40,000” nor the limitation “15,000.”

Conclusion

No claims are allowable.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

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A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

ANY INQUIRY CONCERNING THIS COMMUNICATION OR EARLIER COMMUNICATIONS FROM THE EXAMINER SHOULD BE DIRECTED TO DAVID S. ROMEO WHOSE TELEPHONE NUMBER IS (571) 272-0890. THE EXAMINER CAN NORMALLY BE REACHED ON MONDAY THROUGH FRIDAY FROM 7:30 A.M. TO 4:00 P.M. IF ATTEMPTS TO REACH THE EXAMINER BY TELEPHONE ARE UNSUCCESSFUL, THE EXAMINER'S SUPERVISOR, GARY KUNZ, CAN BE REACHED ON (571) 272-0887.

IF SUBMITTING OFFICIAL CORRESPONDENCE BY FAX, APPLICANTS ARE ENCOURAGED TO SUBMIT OFFICIAL CORRESPONDENCE TO THE FOLLOWING TC 1600 BEFORE AND AFTER FINAL RIGHTFAX NUMBERS:

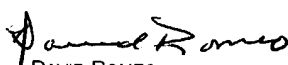
BEFORE FINAL (703) 872-9306

AFTER FINAL (703) 872-9307

CUSTOMERS ARE ALSO ADVISED TO USE CERTIFICATE OF FACSIMILE PROCEDURES WHEN SUBMITTING A REPLY TO A NON-FINAL OR FINAL OFFICE ACTION BY FACSIMILE (SEE 37 CFR 1.6 AND 1.8).

FAXED DRAFT OR INFORMAL COMMUNICATIONS SHOULD BE DIRECTED TO THE EXAMINER AT (571) 273-0891.

ANY INQUIRY OF A GENERAL NATURE OR RELATING TO THE STATUS OF THIS APPLICATION OR PROCEEDING SHOULD BE DIRECTED TO THE GROUP RECEPTIONIST WHOSE TELEPHONE NUMBER IS (703) 308-0196.


DAVID ROMEO
PRIMARY EXAMINER
ART UNIT 1647

DSR
JANUARY 29, 2004